PCN221

IDENTIFICATION OF THE TREATMENT PATHWAY OF METASTATIC CASTRATE-RESISTANT PROSTATE CANCER IN SCOTLAND: A CHART REVIEW

Maman K[1], Khemiri A[2], Roïz J[1], Naidoo S[3], Baskin-Bey E[3], Holmstrom S[4]

[1]*Creativ-Ceutical, London, UK,* [2]*Creativ-Ceutical, Tunis, Tunisia,* [3]*Astellas Pharma Europe Ltd., Chertsey, UK,* [4]*Astellas Pharma Europe, Leiderdorp, The Netherlands*

OBJECTIVES: Chemotherapy with docetaxel was the first therapy approved for the treatment of metastatic Castrate-Resistant Prostate Cancer (mCRPC) while others came along rather recently. With all the treatment options available now, current treatment strategies to appropriately sequence these agents are not known. This study aims to describe mCRPC current treatment paradigms, with specific attention to docetaxel, in Scotland. **METHODS:** A retrospective chart review was conducted. A panel of Scottish physicians was contacted to identify patients diagnosed with mCRPC between 2008 and 2013. Collected data included demographics, disease history, sequencing of therapies (type, duration and time-to-event), reason for switch or discontinuation, drug-related serious adverse events and hospitalisations. Descriptive analyses were performed. Time-to-event was analysed using the Kaplan-Meier method. **RESULTS:** Twelve physicians in Scotland completed the survey and 34 patients were included in the analysis. Mean age at mCRPC diagnosis was 62 years (range 56-69 years). The mean duration between mCRPC diagnosis and the date of last contact was 1.20 years. Postcastration, most patients (19/34, 56%), received docetaxel as first-line. The second most frequent first-line was bicalutamide (14/34, 41%), alone (9/14, 64%) or in combination with LHRHa. Abiraterone was frequently prescribed as next (second or third) line of therapy after docetaxel (6/21, 29%). The median time to switch was 105 days (range 20-235 days) and did not differ between patients with docetaxel versus other as first-line ($p = 0.17$). Most patients switched after radiographic progression or PSA rise. Serious adverse events and hospitalisations were rarely reported. **CONCLUSIONS:** These findings provide insights into the treatment pathway of mCRPC patients in Scotland. Chemotherapy with docetaxel and hormonal agents appear to be the most utilised therapies. Switch from first-line treatment occurred in approximately 3.5 months and was facilitated by radiographic progression or PSA rise. A larger retrospective chart review is needed to confirm these results.

DIABETES/ENDOCRINE DISORDERS – Clinical Outcomes Studies

PDB1

EVALUATION OF ACUTE PANCREATITIS SIGNALS WITH INCRETIN ENHANCERS: REVISITING DISPROPORTIONALITY ANALYSIS OF THE ADVERSE EVENT REPORTING SYSTEM

Ali AK

Eli Lilly and Company, Indianapolis, IN, USA

OBJECTIVES: There has been a rising concern about the association between incretin enhancers and acute pancreatitis (AP). Previous research showed conflicting findings, and this analysis of the FDA Adverse Event Reporting System (FAERS) aims at investigating signals of AP across pharmacological classes of anti-diabetes medications (ADM) and within incretin enhancers class. **METHODS:** Adverse event reports submitted to FAERS between 1997Q3-2012Q1 were analyzed. The outcome was defined by MedDRA Preferred Term (PT) "pancreatitis acute"; exposures were defined by generic names of ADM. Sensitivity analyses were conducted by creating a custom term (CT) for outcome: "autoimmune pancreatitis", "ischemic pancreatitis", "pancreatitis", "pancreatitis acute", "pancreatitis hemorrhagic", and "pancreatitis necrotizing". Reports of other pancreatic disorders were excluded. Disproportionality analysis by proportional reporting ratio (PRR) and 95% confidence interval (LL05-UL95) is applied to detect AP signals compared to all ADM. Associations with LL05≥2 are significant signals. **RESULTS:** A total of1183 AP PT and 4481 CT reports for ADM were identified (incretin enhancers, n=912 and n=3,704, respectively). Corresponding PRR and (LL05-UL95) were: metformin 0.98 (0.83-1.16) and 0.52 (0.47-0.59); sulfonylureas 0.53 (0.37-0.75) and 0.35 (0.28-0.43); thiazolidinediones 0.12 (0.09-0.16) and 0.12 (0.10-0.14); meglitinides 0.54 (0.31-0.93) and 0.39 (0.28-0.54); incretin enhancers 1.94 (1.87-2.00) and 2.09 (2.06-2.12); and combinations 0.65 (0.47-0.88) and 0.81 (0.70-0.93). Compared to all ADM, estimates for incretin enhancers were: exenatide 1.46 (1.37-1.55) and 1.54 (1.49-1.59); liraglutide 4.90 (4.37-5.48) and 4.00 (2.73-4.28); saxagliptin 4.47 (3.00-6.67) and 4.60 (3.73-5.67); and sitagliptin 2.33 (1.95-2.78) and 4.02 (3.75-4.31). There were no reports of AP PT for linagliptin, but 39 reports of CT with estimates of 6.41 (4.64-8.85) were identified. **CONCLUSIONS:** Compared to other ADM, incretin enhancers are associated with higher than expected reporting of AP. Prescribers should monitor patients with diabetes for signs and symptoms of pancreatitis while treated with incretin enhancers. Given limitations of spontaneous reporting systems, pharmacoepidemiological studies are required to test the generated hypothesis and to draw clinically rigorous conclusions.

PDB2

BAYESIAN NETWORK META-ANALYSIS TO ASSESS THE RELATIVE EFFICACY AND SAFETY OF CANAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) INADEQUATELY CONTROLLED ON METFORMIN AND SULPHONYLUREA (MET+SU)

Pacou M[1], Taieb V[1], Abrams KR[2], Diels J[3], van Sanden S[4], Garg M[5], Schroeder M[6], Kaur V[7], Nielsen ATN[5], Nuhoho S[6], Neslusan C[8], Hemels M[5]

[1]*Amaris, London, UK,* [2]*The Institute of Cancer Research, Sutton, UK,* [3]*Janssen Pharmaceutica, Beerse, Belgium,* [4]*EMEA HEMAR Analytics, Janssen EMEA, Beerse, Belgium,* [5]*Janssen Cilag, Birkerød, Denmark,* [6]*Janssen UK, High Wycombe, UK,* [7]*Consultant, Mumbai, India,* [8]*Janssen Global Services LLC, Raritan, NJ, USA*

OBJECTIVES: To assess the relative efficacy and safety of canagliflozin (CANA), a sodium-glucose co-transporter inhibitor, as an add-on to MET+SU, versus DPP-4 inhibitors, GLP-1 agonists and insulin, using Bayesian network meta-analysis (NMA). **METHODS:** A systematic literature review was conducted according to NICE guidelines. Outcomes of interest included HbA1c, weight and hypoglycaemia. A Bayesian NMA using non-informative priors was conducted, based on linking trials with treatment and dose-specific common treatment arms. Assessment of model fit and selection of fixed versus random effects was based on the Deviance Information Criterion (DIC). Sensitivity analyses assessed the impact of individual trials and definition of priors. Consistency between direct and indirect evidence was assessed. **RESULTS:** Ten studies reporting results at 26 weeks +/- 4 weeks were identified. HbA1c-reduction (D) for CANA 100mg was comparable to DPP-4s (D between 0.05 and -0.14 versus sitagliptin and linagliptin respectively, with pairwise probabilities (P) of being more effective between 33-88%), and higher for CANA 300mg, which was comparable to GLP-1s (D=0.08;P=31% and 0.01;P=53%) versus liraglutide 1.8mg and exenatide 10µg respectively) and biphasic insulin (D=0.03;P=43%). CANA 300mg had the highest weight reduction with changes between 0.14kg;P=93% (vs. exenatide 10µg) and 5.13kg;P=100% (vs. biphasic insulin). The odds ratio for hypoglycaemia versus long-acting insulin were 0.31 and 0.39 for CANA 100mg and 300mg respectively, compared to 0.20-0.41 for other classes. **CONCLUSIONS:** NMA of add-on therapies to MET+SU suggests that glycaemic reductions for CANA at 26 weeks are at least as large for CANA 100 mg and greater for CANA 300 mg compared to DPP-4s. CANA 300mg was found to be comparable to liraglutide 1.8mg and biphasic insulin. Weight reduction was similar to GLP-1s and substantially higher compared to all other classes. All classes showed significantly lower hypoglycaemic event rates compared to insulin.

PDB3

COMPARATIVE EFFECTIVENESS OF LIRAGLUTIDE VERSUS SITAGLIPTIN IN TYPE 2 DIABETES IN THE UNITED KINGDOM: A RETROSPECTIVE STUDY IN PRIMARY CARE

Nyeland ME[1], Ploug UJ[1], Skovgaard R[1], Richards A[1], Bergan EQ[1], Zammit DC[2], Evans M[3]

[1]*Novo Nordisk A/S, Søborg, Denmark,* [2]*IMS Health, Basel, Switzerland,* [3]*University Hospital Llandough, Cardiff, UK*

OBJECTIVES: Liraglutide is an incretin-based (GLP-1 analog) therapy indicated for the treatment of patients with type 2 diabetes (T2DM). This study aimed to assess whether phase 3 clinical trial data, showing significantly greater reductions in HbA1c and body weight vs. the DPP-IV inhibitor sitagliptin is translated into routine clinical practice. **METHODS:** This was a retrospective database analysis of the Clinical Practice Research Datalink (CPRD), a primary care database in the UK. Patients (≥18 years) diagnosed with T2DM and prescribed liraglutide or sitagliptin between July 2009 and July 2012, were included. Patients on insulin or fixed dose metformin combinations at therapy initiation were excluded. Outcomes included: % of patients achieving ≥1% HbA1c reduction; % of patients with HbA1c reduction ≥1% and weight reduction ≥3% (NICE criteria); % of patients achieving treatment target HbA1c <7%; absolute change in HbA1c, weight (BMI), systolic blood pressure and blood lipids. **RESULTS:** Baseline demographics: 294 liraglutide and 2790 sitagliptin patients with a mean age of 55.7 (SD 10.6) and 62 (SD 11.0) years and 36.4% and 40.5% female respectively. Patients had a baseline HbA1c of 8.9% (SD 1.9) and 8.6% (SD 1.5), a baseline BMI of 39.3 (SD 7.1) and 33.3 (SD 6.4) and had been diagnosed with diabetes 7.1 and 7.2 years prior to start of current treatment for liraglutide and sitagliptin respectively. Comparative effectiveness analysis demonstrated superior reductions for liraglutide vs. sitagliptin in HbA1c (%) (-0.89 vs. -0.57, p<.01), weight (Kg) (-3.78 vs. -1.12, p<.0001), BMI (-1.3 vs. -0.4, p<.0001) and systolic blood pressure (mmHg) (-4.1 vs. -0.37, p<.0005) after 6 months of therapy. No statistically significant differences were observed in total cholesterol and HDL reductions. **CONCLUSIONS:** The superior control and weight reduction of liraglutide vs. sitagliptin observed in clinical trials is reflected in routine primary care clinical practice.

PDB4

WEIGHT LOSS OF ≥3% IN TYPE II DIABETES PATIENTS IS ASSOCIATED WITH WEIGHT CHANGE PROPERTY OF NEWLY PRESCRIBED ANTI-DIABETIC MEDICINE IN ANTI-DEPRESSANT USERS OVER A 12-MONTH FOLLOW-UP PERIOD

Lin CC[1], Mukherjee J[2], Kawabata H[3], Colilla S[3], Wygant G[4]

[1]*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA,* [2]*Bristol-Myers Squibb, Wallingford, CT, USA,* [3]*Bristol-Myers Squibb, Hopewell, NJ, USA,* [4]*Bristol-Myers Squibb, Princeton, NJ, USA*

OBJECTIVES: Anti-depressant use could complicate the weight change effect of anti-diabetes (AD) medications. This study examined if different newly prescribed AD medications were associated with weight loss in a 12-months period in type II diabetes (T2D) patients who were on anti-depressants. **METHODS:** The study included patients who were on anti-depressants (selective serotonin reuptake inhibitors, SSRI, or tricyclic antidepressants,TCA) and prescribed a new AD during 1995-2011 from the UK Clinical Practice Research Datalink (CPRD.) Patients on more than one ADs are included if ADs are within same weight-change category, categorized as weight-gain agents (WG)(sulfonylureas (SU), thiazolidinediones (TZD)) and weight- neutral/ loss agents (WN/L)(metformin(MET), DPP-4 inhibitors (DPP-4), GLP-1 agonists (GLP-1). Descriptive analyses and multivariate regression examined the association between weight loss ≥3% and newly prescribed AD medications grouped by weight change category. **RESULTS:** This study included 3,445 T2D patients, of whom 2,041 were SSRI users and 1,404 were TCA users. Mean (sd) age was 60(±13.2) years for SSRI users and 64(±12.0) years for TCA users. Baseline mean (sd) weight was 92.86(±22.24) kg for SSRI users and 89.31(±19.86) kg for TCA users. At 12 months after initiation of AD therapy, with baseline age, weight, and other characteristics controlled, the likelihood of achieving weight loss of ≥3% was higher for those prescribed a WN/L agents versus those prescribed a WG agents regardless of the anti-depressant medicine currently used: For SSRI users OR= 2.84; 95% CI [1.89, 4.32]; for TCA users OR = 1.51; 95% CI [1.03, 2.23]. **CONCLUSIONS:** T2D anti-depressant users prescribed WN/L agents had higher odds of actual weight loss of ≥3%, compared to those prescribed WG agents. This association holds regardless of the anti-depressant medicine patients are currently taking. For T2D patients on anti-depressants, considering different weight change effects when initiating anti-diabetes therapy is needed.